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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/259,658	02/26/1999	JOHN COLYER	04256/79245	5554

29933 7590 07/06/2005

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/259,658	COLYER ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/7/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,18,21-38 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,18,21-31,34-38 and 41* is/are rejected.

7)☒ Claim(s) *24,32 and 33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 17-18,21-38 and 41 are pending.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

1. **(Withdrawn**; claims have been canceled.) New Claims 39 and 40 depend from claims 22 and 23, respectively and are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim Rejections - 35 USC § 112

2. **(Withdrawn**; claims have been canceled.) Claims 39 and 40 rejected under 35 U.S.C. 112, second paragraph for reciting the term "proteolysis", this term lacks antecedent basis in claims 22 and 23 from which claims 39 and 40 depend.
(Withdrawn in light of the amendment of claim 17, to clarify the binding to be dependent upon the presence or absence of the modification) Claim 17 rejected under 35 U.S.C. 112, second paragraph for reciting the recitation of "and the reversal of these covalent modifications".

3. **(Withdrawn**, as the claims have been amended to recite "further comprises a label") Claims 24 and 27 rejected under 35 U.S.C. 112, second paragraph for not reciting ---- further comprising a radioactively or fluorescently labeled polypeptides--- .

4. **(Withdrawn)** (method) Claims 18, 21-33, 36-40 (high throughput; title, "real time" assay) under 35 U.S.C. 102(e) as being anticipated by Wagner et al (US Pat. 6,475,809, effective filing date July 14,1998) is herein withdrawn in light of the newly submitted combination of claim limitations.

5. **(Withdrawn)** Claims 22-23, 39-40 (proteolysis species) rejected under 35 U.S.C. 102(e) as being anticipated by Shone et al (US Pat. 5,962,637,. filing date December 3, 1996), in light of the newly submitted combination of claim limitations submitted.

Response to Arguments

6. Applicant's arguments filed 5/9/2005 have been fully considered but they are not persuasive.

7. **(Maintained)** The rejection of claim 17 under 35 U.S.C. 102(b) as being anticipated by Fitzpatrick et al (US Pat. 5,710,009) was traversed on the grounds that the

modification recited in the claims requires a covalent modification, and that the complex of claim 17, as amended defines over Fitzpatrick.

8. It is the position of the examiner that Fitzpatrick et al disclose and claim a composition that comprises an immobilized complex (see claim 19) that comprises the combination of first and second polypeptides, specifically a peptide "reland" (col. 5, lines 4-6, line 22) together with its receptor (see col. 5, lines 54-60), wherein the two polypeptides of Fitzpatrick et al of (Example 3, col. 27) are the combination of a deglycoslyated hemoglobin and an antibody that binds to covalently modified/glycosylated hemoglobin .

9. The two polypeptides are utilized in a method for detecting glycosylated hemoglobin. Glycosylation and deglycosylation are two claimed species of instant amended claim 17, and the composition of Fitzpatrick et al (claim 19) includes the disclosed embodiment exemplified in Example 3, which is directed to complexes for the detection of differential glycosylation patterns, which include deglycosylation and glycosylation binding partners immobilized on a support together with an antibody that is specific for a glycoslyation epitope of hemoglobin ('009, col. 10, lines 61-65; col. 27, Example 3 and claim 19). The reference still anticipates the instantly claimed invention as now claimed.

10. **(Maintained)** The rejection of (composition) claim 17 under 35 U.S.C. 102(b) as being anticipated by Hochstrasser et al (US Pat. 5,565,352) is traversed on the grounds that Hochstrasser et al does not disclose a composition of amended claim 17 and does not read on a ubiquitin covalent attached to the other polypeptide.

11. It is the position of the example that the immobilized complex (see Figure 6a) was the combination of first and second polypeptides. The first polypeptide being an ubiquitin-oligopeptide covalent conjugate and the second polypeptide being an anti-ubiquitin antibody polypeptide. (see col. 1, lines 23-25, and lines 26-45)

12. (see Figures 6a and 6b) The immobilized ubiquitin-oligopeptide covalent conjugate formed a complex on a solid immunoblot surface when immunoreacted with an anti-ubiquitin antibody polypeptide; also see col. 6, lines 63-67 and col. 7, lines 1-16; Example 4, col. 40, lines 14-56). The reference still anticipates the instantly claimed complex that comprises first and second polypeptides to comprise a covalent modification, specifically ubiquitination, in order to form a complex.

13. (**Maintained**) The rejection of (method) claims 18, 21-26,31, and 34-38 under 35 U.S.C. 102(b) as being anticipated by Hochstrasser et al (US Pat. 5,565,352) is traversed on the grounds that:

the claims require the presence of distinct elements and Hoschstrasser et al does not disclose the combination of all of the elements.

14. It is the position of the examiner that Hoshstrsser et al disclose an assay of a polypeptide substrate modified by polyubiquitin, which is proteolytically digested and further modified by the disclosed deubiquitination enzyme (see Figure 6b).

15. The assay for agonists/antagonists/modulators (see col. 25, lines 30-51) of activity are disclosed to include a candidate substance (see col. 26, lines 13-15) which are combined with the first polypeptide, a substrate second polypeptide/protein, co-factors, relevant modifications such as glycosylation or prenylation.

16. The **first polypeptide**, deubiquitin is disclosed for immobilization on a solid support (see col. 26, lines 66-67 bridging to col. 27, lines 1-5).

17. Among the disclosed **second polypeptide** are "short-lived eukaryotic proteins,

Among the defined polypeptides that are short lived proteins are:

cyclins, c-mos protein kinase ; MATα2 (see col. 33, lines 30-43). The modifying enzyme which attaches ubiquitin to the substrate protein/polypeptide is E2 enzymes (see col. 33, lines 53-59).

E2 enzymes (see col. 33, lines 55-59) are modifying enzymes that covalently attach and modify the second short lived polypeptide with ubiquitin (see col. 33, lines 29-31). The combination of polypeptide-ubiquitin conjugate defines a species of second polypeptide disclosed in '352; the conjugate being made through the action of a modification enzyme E2 (adds ubiquitin to a polypeptide) and the modifying substrate.

Other modifying enzymes disclosed include enzymes that add a covalent modifying group, specifically a glycosylation or prenylation group (see col. 26, lines 32-33) .

After combining all the essential components to obtain a base line (first polypeptide) enzyme activity (see col. 27, lines 18-21), an admixture of an inhibitor, modifier, candidate modulator compound for the enzyme (first polypeptide) function (see col. 27, lines 48-57) is added to the reaction assay system (see col. 27, lines 18-47).

Also the presence of relevant co-factors and relevant modifications (see c. 26, lines 31-42), as well as labels and detection reagents (see col. 28, lines 16-59) are provided. The reference still anticipates the instantly claimed invention.

FP*	SP*	MGS*	modifying*
Enzyme (col. 26,l. 28-29)	protein substrate (c.26,l.29)	glycosylation	glycosylating E (c. 26,l.32-33)
Enzyme(c. 26, l.28-29)	protein substrate (c.26,l.29)	prenylation	prenylating E (c. 26,l. 32-33)
Enzyme	Short lived protein substrate polypeptide	Ubiquination	E2 enzyme (c.33,l. 58)

l.:line c or col.:column E. enzyme

FP: immobilized first polypeptide

SP: second polypeptide

MGS: modifying group substrate

Modifying: modifying agent

New Grounds of Objection/Rejection

Allowable Subject Matter

18. Claims 32-33 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Objections

19. Amended Claim 24 is objected to because of the following informalities: Claim 24 has been amended to recite the phrase "polypeptides labeled further comprises a label"; the first recitation of "labeled" should be removed. Appropriate correction is required.

Claim Rejections - 35 USC § 112

20. Claim 21 recites the limitation "test sample" in reference to the term "sample". There is insufficient antecedent basis for the limitation "test" in the claim, which does not define the sample to be a test sample.

Claim Rejections - 35 USC § 102

21. Amended and New Claims 17 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Avruch et al (US Pat. 5,582,995) in light of Avruch et al (US Pat. 5,736,337) who provides evidence that Ras/Raf binding is effected by phosphorylation, and dephosphorylation (see '337, col. 20, lines 1-15).

Avruch et al disclose the instantly claimed invention directed to a polypeptide pair comprising a first polypeptide immobilized to a support and a second polypeptide bound to the firs polypeptide, wherein binding of the two polypeptide is detectable.

Avruch et al disclose an immobilized polypeptide pair complex, the first polypeptide being Ras or a Raf-bining fragment thereof bound to Raf or a Ras-binding fragment thereof (see col. 14, lines 13-21).

Avruch et al disclose a polypeptide pair comprising :

A **first polypeptide** immobilized to the support (either Raf (a kinase, see col. 13, line 20)) or Ras (see col. 13, lines 40-60); and

A **second binding partner polypeptide** bound to the first polypeptide (if Raf is immobilized then Ras is the second binding partner polypeptide or if Ras is immobilized then Raf is the second binding partner polypeptide (see col. 6, lines 1-65)) , wherein modulation of binding is effected by a covalent modification, the covalent modification

(see col. 16, lines 25-35 "acetylation or carboxylation", "glycosylation", "deglycoylationg", "phosphorylated") being a phosphate group results in phosphorylation , the complex being immobilized through binding the first and second polypeptide to each other (see col. 16, lines 64-67 and col. 17, lines 1-3) and to a solid phase by the first polypeptide, wherein the binding of the first and second polypeptides is detectable with a monoclonal antibody (see col. 4, lines 58-59), or the second polypeptide is labeled (see col. 13, lines 64-65)

The immobilized complex the comprises first and second polypeptides of a polypeptide pair of Avruch et al inherently anticipates the instantly claimed invention in light of the evidence provided by Avruch et al '337 that shows modulation of binding between the two polypeptides based upon phosphorylation (see'337, col. 20, lines 1-15), and dephosphorylation would modulate binding.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states AArtisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art s functioning, does not render the old composition patentably new to the discoverer. AThe Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

22. (Composition claims) Claim 17 and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Beach et al (effective filing date October 24, 1994).

Beach et al disclose a polypeptide pair comprising :

A **first polypeptide** immobilized to the support (either Raf (a kinase)) or CDC25 (a phosphatase , see col. 9, line 44) , see col. 10, lines 35-57 and col. 11, lines 1-50); and

A **second binding partner polypeptide** bound to the first polypeptide (if Raf is immobilized then CDC25 is the second binding partner polypeptide or if CDC25 is immobilized then Raf is the second binding partner polypeptide) , wherein modulation of binding is effected by a covalent modification, the covalent modification being the transfer of a phosphate group (ATP) which results in phosphorylation (see col. 6, lines 15-29, col. 6, lines 56-61; col. 12, lines 55-60 (reaction mixture includes ATP);

Wherein Raf kinase binds to CDC25 phosphatase through the addition of a phosphate group, a covalent modification, resulting in phosphorylation of CDC25 (see col. 9, lines 40-45).

Beach et al disclose the instantly claimed invention directed to an immobilized polypeptide pair, the pair including the complex of Raf/CDC25. The polypeptide pair of Beach et al anticipates the instantly claimed invention as now claimed.

23. (Methods) Claims 18, 21-27 and 31, are rejected under 35 U.S.C. 102(e) as being anticipated by Beach et al (US Pat. 6,037,136, effective filing date October 24, 1994).

24. Beach et al disclose the instantly claimed invention of claim 18 (see col. 11, lines 14-22; and lines 52-67 and col. 12, lines 1-60), the method comprising the steps of:

Providing a first immobilized polypeptide on a support (the polypeptide being Raf or CDC25, col. 10, lines 35-36 or MAPK/ERK kinase col. 13, lines 64-67 and col. 14, lines 1-5 or PDGF/Ras and CDC25 (see col. 17, lines 53-59; see col. 10, line56 "beads"; lines 66-67 "immobilized proteins on matrices", col. 10, line 49 "microtitre plates"; col. 10, lines 42-43 "microtitre plates, test tubes and micro-centrifuge tubes"col. 11, lines 1-2");

Providing a second polypeptide (ie: Raf or CDC2), the association being modulated by a covalent modification (phosphate, see Col. 26, Example 4, lines 17-29) and

Allowing the polypeptides to bind to each other (Raf/CDC25 complexes, see Examples 4-5 and all claims) ,

Contacting the polypeptides with a modification enzyme (examples disclosed include Ras1 kinase which modifies CDC25 (see col. 12, line 1); or CDK/cyclin that modifies histones to produce phosphorylated histones (see col. 12, lines 30-34) ;or MEK, MAPK or bcL1-2 (see col. 14, lines 1-5)) which in the presence of said modifying group substrate ,the substrate (see col. 12, lines 19-30 and lines 31-36) being phosphorylation of histones by the activated CDK modifying enzyme or (Rb where CDK4 or CDK6 are used); the reaction mixture including ATP (see col. 12, line 60);

Detecting modulation of the binding of the polypeptides to determine a reference signal modulation (see "The ability of a test agent to inhibit the activation of CDC25 enzyme is therefore manifest by a decrease in DCK activation as compared to the system in the Absence of the test agent (see col. 12, lines38).

Detecting modulation of binding of the polypeptides in the presence of said candidate modulator (see col. 12, lines 5-18 control and test assay systems; col. 9, lines 54-63 "drug screening programs", "high throughput assays"; col. 12, lines 35-38 "test agent"; col. 11, lines 52-67 "activation (or inactivation)", "Inhibitors (and potentiatorS)" and col. 12, lines 1-18) and comparing the modulation

detected in the presence and absence of the candidate modulator (see col. 10, lines 9-20, "dose response curves" of the test compound compared with a "baseline for comparison"; compared to the system in the absence of the test agent(col. 12, lines 33-34); col. 14, line 5"presence or absence of a test compound").

Instant claim 24: at least one of the polypeptides comprises a label (see col. 10, lines 23-50).

Instant claim 25: the label comprises a fluorescent label (see col. 10, line 28).

Instant claim 26: the label comprises a radioactive label (see col. 10, line 27).

Instant claim 27: both polypeptides comprise a label (see claim 6 "both are fusion proteins" the fusion portion being a type of label).

Instant claim 31: the association is measured by monitoring molecular mass (see col. 10, lines 60-62 "SDS-PAGE" gel electrophoresis separates polypeptides based upon molecular mass and charge).

The reference anticipates the instantly claimed invention as now claimed.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 18,21-25, 34-35 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. US Pat. 6,656,696. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

4. the allowed claims are directed to a species of covalent modification, specifically phophorylation through enzymatic activity of a kinase or phosphatase , and the instantly claimed methods are directed to the evaluation of any enzymatic medication to include phophorylation, acylation, glycoylation, ubiquitination, prenylation, sentrinization and ribosylation, and the definition of the method of the allowed claims include in-vitro methods (see '696, col. 16, line 7), the invitro methods including the immobilization of the first and second polypeptides("western blot" col. 2, lines 17-19 and lines 23-26; "captured on cation exchange filter paper" col. 25, lines 8-25 and in SDS-PAGE gel pieces; '696, col. 36, lines 35-38 cells provided on solid culture medium) and the first and second polypeptides are referred to as a natural binding domain and binding partner ('696, figures 1-2; col. 4, lines 40-67; and col. 19, lines 60-65), therefore the allowed species of invention anticipates the instantly claimed genus of methods.

5. Claim 18 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. US Pat. 6,670,144. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

6. the allowed claims are directed to a species of covalent modification, specifically phophorylation through enzymatic activity of a kinase or phosphatase , and the instantly claimed methods are directed to the evaluation of any enzymatic medication to include phophorylation, acylation, glycoylation, ubiquitination, prenylation, sentrinization and ribosylation, and the definition of the method of the allowed claims include in-vitro methods (see '144, col. 24, line 3, the invitro methods including the immobilization of the first and second polypeptides("western blot"; "captured on cation exchange filter paper" and in SDS-PAGE gel pieces; as well as cells provided on solid culture medium) and the first and second polypeptides are referred to as a natural binding domain and

binding partner ('144, figures 1-2; col. 25, lines 30-40), therefore the allowed species of invention anticipates the instantly claimed genus of methods.

7. Claims 18, 21-25, and 34-35 are is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. US Pat. 6,465,199. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

8. the allowed claims are directed to a species of covalent modification, specifically modifications other than kinase and phosphatase, and

9. the instantly claimed methods are directed to the evaluation of any enzymatic medication to include phophorylation, acylation, glycoylation, ubiquitination, prenylation, sentrinization and ribosylation and are therefore broader in scope than the allowed claims.

10. The definition of the method of the allowed claims of US Pat. 6,465,199 include in-vitro methods, the in-vitro methods including the immobilization of the first and second polypeptides ("western blot"; "captured on cation exchange filter paper" and in SDS-PAGE gel pieces; as well as cells provided on solid culture medium) and the first and second polypeptides (see '199, Figures 1-2) are referred to as a natural binding domain and binding partner , therefore the allowed species of invention anticipates the instantly claimed genus of methods that include post-translational modifications by kinase and phosphatase enzymes, as well as by other enzymes.

11. Claims 21-30,34-35 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over allowed claims 1-2, 4-8, 10-14 of U.S. Patent Application 09/511,776. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

12. the allowed claims are directed to a species of covalent modification, specifically polypeptides that are post-translationally modified with a Kinase or Phosphatase (see 09/511,776, Specification page 26, lines 22-23 and Figure 4, phosphorylation) enzyme which results in the non-covalent binding of the first and second polypeptides one to the

other , and the instantly claimed methods allow the binding of the first and second polypeptides to be either covalent or non-covalent in nature, but binding of the first and second polypeptides is modulated by the activity of the modifying enzyme, the activity of which is being measured in the claimed methods. Therefore the allowed claims are directed to a species of invention which anticipates the instantly claimed genus of methods.

Conclusion

13. ***This is a non-final action.***

25. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

26. Amersham Life Science is cited to show Spa cytostar Proximity News Scintillation Proximity Assay (SPA) Bibliography, Issue No 35, Nov. 1997 and is covered by US Pat. 5,665,562.
27. Kohl, Nancy (Annals of New York Academy of Sciences) is cited to show methods for the development of farnesyltransferase inhibitors
28. Lebowitz et al (1995) is cited to show inhibitors for farnesyltransferase that suppress transformation by interfering with Rho activity, as well as an assay.
29. Leftheris et al (1996) is cited to show the development of highly potent inhibitors of Ras Farnesyltransferase possessing cellular and in vivo activity.
30. Qian et al (1997) is cited to show Farnesyltransferase as a target for anticancer drug design (see page 28, and Figure 5).
31. US Pat. 5,185,248 is cited to show an assay that comprises an immobilized polypeptide substrate for screening farnesyl protein transferase (see claim 19).
32. US Pat. 5,789,541 (Rando) is cited to show compounds for inhibition of proteolysis, wherein farnesyltransferase comprises two polypeptides of 43 kDa and 34 kDa (claim 1).
33. US Pat. 5,578, 477 is cited to show a method for identificaon of inhibitors of protein farmesyltransferase.
34. US Pat. 5,990,277 (Levitzki et al) is cited to show inhibits farnesyl protein transferase.
35. US Pat. 6,261,793 (Whyte et al) is cited to show a method of identifying inhibitors of endoprotease activity associated with human Ras converting enzyme.
36. US Pat. 6,117,641 (Berlin et al) is cited to show an assay for inhibitors of geranylgeranyl transferase I (see claims 24-26).
37. US Pat. 6,189,362 (Duchesne et al) is cited to show peptides that inhibit the transforming activity of activated p21 proteins (see all claims)

38. US Pat. 6,410,255 (Pollok et al) is cited to show a method of measuring post-translational modification activity of an protease (see all claims, especially claim 6 "attached to a solid").
39. US Pat. 5,637,463 (Dalton et al) is cited to show a method of detecting protein-protein interactions, effected by posttranslational modification (see title, abstract).
40. WO90/14431 is cited to show fusion proteins that comprise a post-translational modification site, that are immobilized by binding to avidin (see claim 28).
41. Cyclacel Ltd. Patents (US Pat. 6,808,874; 6,569,833; 6,613,878) are cited to show methods for screening candidate compounds that modulate interactions between a binding partner and binding domain in the presence of a covalent modifying enzyme.

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
June 28, 2005

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